Complete Summary

GUIDELINE TITLE

Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update.

BIBLIOGRAPHIC SOURCE(S)

Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum 2000 Sep;43(9):1905-15. [91 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Osteoarthritis of the hip and knee

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management

CLINICAL SPECIALTY

Family Practice
Geriatrics
Internal Medicine
Orthopedic Surgery
Physical Medicine and Rehabilitation
Rheumatology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To present evidence-based recommendations for the medical management of osteoarthritis of the hip and knee

TARGET POPULATION

Patients with osteoarthritis of the hip and/or knee

INTERVENTIONS AND PRACTICES CONSIDERED

Nonpharmacologic therapy

1. Patient education
2. Self-management programs (e.g., Arthritis Foundation Self-Management Program)
3. Personalized social support through telephone contact
4. Weight loss (if overweight)
5. Aerobic exercise programs
6. Physical therapy
7. Range-of-motion exercises
8. Muscle-strengthening exercises
9. Assistive devices for ambulation
10. Patellar taping
11. Appropriate footwear
12. Lateral-wedged insoles (for genu varum)
13. Bracing
14. Occupational therapy
15. Joint protection and energy conservation
16. Assistive devices for activities of daily living

Pharmacologic therapy

1. Oral:
    a. Acetaminophen
    b. Cyclooxygenase 2 (COX-2)-specific inhibitor
    c. Nonselective nonsteroidal antiinflammatory drug (NSAID) plus misoprostol or a proton pump inhibitor
    d. Nonacetylated salicylate
    e. Other pure analgesics – Tramadol, Opioids
2. Intraarticular:
    a. Glucocorticoids
    b. Hyaluronan
3. Topical:
    a. Capsaicin
    b. Methylsalicylate

Referral to orthopedic surgeon, as indicated for surgery

Note: Several agents were considered but not recommended because the agents were still under investigation or lacked evidence. These agents include; glucosamine and chondroitin; dietary supplementation, acupuncture, disease-modifying osteoarthritis drugs, autologous chondrocyte transplantation, cartilage repair using mesenchymal stem cells, and autologous osteochondral plugs (mosaicplasty).

MAJOR OUTCOMES CONSIDERED

- Efficacy of treatment in controlling pain, improving function and health-related quality of life
- Toxic effects of therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The strongest weight was given to data from systematic reviews, meta-analyses, and published findings of randomized controlled trials; data from randomized controlled trials presented as abstracts at scientific meetings were also considered. Where such data were not available, however, the subcommittee followed the approach taken by the Agency for Health Care Policy and Research, as outlined in the American College of Rheumatology (ACR) document "Guidelines for the Development of Practice Guidelines," (see "Companion Documents") which combines a detailed, evidence-based approach with a process that accommodates expert opinion.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Studies of the results of monthly telephone calls by trained nonmedical personnel to discuss such issues as joint pain, medications and treatment compliance, drug toxicities, date of next scheduled visit, and barriers to keeping clinic appointments showed moderate-to-large degrees of improvement in pain and functional status without a significant increase in costs.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC):

<u>Nonpharmacologic Modalities</u>

The components of nonpharmacologic therapy are outlined in the section titled "Nonpharmacologic Therapy for Patients with Osteoarthritis", below. Patient education and, where appropriate, education of the patient's family, friends, or other caregivers are integral parts of the treatment plan for patients with osteoarthritis. Patients should be encouraged to participate in self-management programs, such as the Arthritis Foundation Self-Management Program. Additional educational materials, including videos, pamphlets, and newsletters, are available from the Arthritis Foundation and other national voluntary health organizations. Another cost-effective nonpharmacologic approach for patients with osteoarthritis is provision of personalized social support, either directly or by periodic telephone contact.

Individuals with osteoarthritis of the lower extremity may have limitations that impair their ability to perform activities of daily living (ADLs), such as walking,

bathing, dressing, use of the toilet, and performing household chores. Physical therapy and occupational therapy play central roles in the management of patients with functional limitations. The physical therapist assesses muscle strength, joint stability, and mobility; recommends the use of modalities such as heat (especially useful just prior to exercise); instructs patients in an exercise program to maintain or improve joint range of motion and periarticular muscle strength; and provides assistive devices, such as canes, crutches, or walkers, to improve ambulation. Similarly, the occupational therapist can be instrumental in directing the patient in proper joint protection and energy conservation, use of splints and other assistive devices, and improving joint function. In addition, the input of a vocational guidance counselor may be important to patients who are still actively employed.

Quadriceps weakness is common among patients with knee osteoarthritis, in whom it had been believed to be a manifestation of disuse atrophy, which develops because of unloading of the painful extremity. Recent studies, however, have indicated that quadriceps weakness may be present in persons with radiographic changes of osteoarthritis who have no history of knee pain, and in whom lower extremity muscle mass is increased, rather than decreased; and that quadriceps weakness may be a risk factor for the development of knee osteoarthritis, presumably by decreasing stability of the knee joint and reducing the shock-attenuating capacity of the muscle.

The beneficial effects of both quadriceps strengthening and aerobic exercise for patients with knee osteoarthritis, noted in the original recommendations, were confirmed in the Fitness Arthritis and Seniors Trial (Ettinger WH Jr, Bums R, Messier SP, Applegate W, Rejeski WJ, Morgan T, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis: the Fitness Arthritis and Seniors Trial [FAST]. JAMA 1997;277:25-31). The ability of elderly subjects to maintain conditioning levels of exercise is noteworthy, since many patients with advanced hip or knee osteoarthritis are sedentary, deconditioned, and at increased risk for cardiovascular disease.

The 1995 American College of Rheumatology guidelines also recommended that overweight patients with hip or knee osteoarthritis lose weight (Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthritis Rheum 1995 Nov;38[11]:1535-40; Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthritis Rheum 1995 Nov;38[11]:1541-6).

As noted in the 1995 American College of Rheumatology recommendations, proper use of a cane (in the hand contralateral to the affected knee) reduces loading forces on the joint and is associated with a decrease in pain and improvement of function. In addition, patients may benefit from wedged insoles to correct abnormal biomechanics due to varus deformity of the knee. Another useful maneuver for patients with osteoarthritis of the knee who have symptomatic patellofemoral compartment involvement is medial taping of the patella.

Nonpharmacologic Therapy for Patients with Osteoarthritis:

- Patient education

- Self-management programs (e.g., Arthritis Foundation Self-Management Program)
- Personalized social support through telephone contact
- Weight loss (if overweight)
- Aerobic exercise programs
- Physical therapy
- Range-of-motion exercises
- Muscle-strengthening exercises
- Assistive devices for ambulation
- Patellar taping
- Appropriate footwear
- Lateral-wedged insoles (for genu varum)
- Bracing
- Occupational therapy
- Joint protection and energy conservation
- Assistive devices for activities of daily living

Pharmacologic therapy

All of the pharmacologic agents discussed in this section should be considered additions to nonpharmacologic measures, such as those described above, which are the cornerstone of osteoarthritis management and should be maintained throughout the treatment period. Drug therapy for pain management is most effective when combined with nonpharmacologic strategies.

For many patients with osteoarthritis, the relief of mild-to-moderate joint pain afforded by the simple analgesic, acetaminophen, is comparable with that achievable with a nonsteroidal anti-inflammatory drug.

Although a number of patients may fail to obtain adequate relief even with full doses of acetaminophen, this drug merits a trial as initial therapy, based on its overall cost, efficacy, and toxicity profile. In patients with knee osteoarthritis with moderate-to-severe pain, and in whom signs of joint inflammation are present, joint aspiration accompanied by intraarticular injection of glucocorticoids or prescription of a nonsteroidal anti-inflammatory drug merits consideration as an alternate initial therapeutic approach.

The daily dose of acetaminophen should not exceed 4 gm. Although it is one of the safest analgesics, acetaminophen can be associated with clinically important adverse events.

For those patients who fail to obtain adequate symptomatic relief with the above measures, alternative or additional pharmacologic agents should be considered. The choice should be made after evaluation of risk factors for serious upper gastrointestinal (GI) and renal toxicity.

Additional considerations involved in a practitioner's decision to treat the individual osteoarthritis patient include existing comorbidities and concomitant therapy, as well as the side effects and costs of specific treatments. In individuals with osteoarthritis of the knee who have mild-to-moderate pain, do not respond to acetaminophen, and do not wish to take systemic therapy, the use of topical analgesics (e.g., methylsalicylate or capsaicin cream) is appropriate as either

adjunctive treatment or monotherapy. Capsaicin cream should be applied to the symptomatic joint 4 times daily; a local burning sensation is common, but rarely leads to discontinuation of therapy. A systematic review of topical nonsteroidal anti-inflammatory drugs also demonstrated efficacy in patients with osteoarthritis; there are no published findings of trials comparing the same nonsteroidal anti-inflammatory drug administered orally versus topically.

Pharmacologic Therapy for Patients with Osteoarthritis*:

- Oral
    - Acetaminophen
    - Cyclooxygenase 2 (COX-2)-specific inhibitor
    - Nonselective nonsteroidal antiinflammatory drug (NSAID) plus misoprostol or a proton pump inhibitor**
    - Nonacetylated salicylate
    - Other pure analgesics
        - Tramadol
        - Opioids
- Intraarticular
    - Glucocorticoids
    - Hyaluronan
- Topical
    - Capsaicin
    - Methylsalicylate

* The choice of agent(s) should be individualized for each patient as noted in the original guideline document text. COX-2 = cyclooxygenase 2; NSAID = nonsteroidal antiinflammatory drug.
** Misoprostol and proton pump inhibitors are recommended in patients who are at increased risk for upper gastrointestinal adverse events.

Initiation of Treatment in the Patient at Increased Risk for an Upper Gastrointestinal Adverse Event

The options for medical management of osteoarthritis that has not responded to the above measures in patients who are at increased risk for a serious upper gastrointestinal adverse event, such as bleeding, perforation, or obstruction, are summarized in the section titled "Pharmacologic Therapy for Patients with Osteoarthritis", above; these include either oral agents or local intraarticular therapy. Two cyclooxygenase 2 (COX-2)-specific inhibitors, celecoxib and rofecoxib, have been studied in patients with osteoarthritis. Celecoxib has been found to be more effective than placebo and comparable in efficacy with naproxen in patients with hip or knee osteoarthritis. Rofecoxib has also been found to be more effective than placebo and is comparable in efficacy with both ibuprofen and diclofenac in patients with hip or knee osteoarthritis. Endoscopic studies have shown that celecoxib and rofecoxib are both associated with an incidence of gastroduodenal ulcers lower than that of the comparator nonsteroidal anti-inflammatory drugs and similar to that of placebo. These data suggest an advantageous safety profile compared with that of nonselective nonsteroidal anti-inflammatory drugs, especially for treatment of high-risk patients. However, the results of large, long-term studies that were designed to demonstrate differences between cyclooxygenase 2 -specific inhibitors and nonselective nonsteroidal anti-

inflammatory drugs with respect to major gastrointestinal clinical outcomes have not yet been published. Such studies have been completed, and results were expected to be published some time in 2000.

Of further advantage with respect to upper gastrointestinal bleeding, neither of the cyclooxygenase 2-specific inhibitors has a clinically significant effect on platelet aggregation or bleeding time. This is a consideration, especially in pre- and perioperative management of patients with osteoarthritis (in whom nonselective nonsteroidal anti-inflammatory drugs have traditionally been discontinued as long as 2 weeks prior to surgery), as well as for patients taking warfarin sodium. Accordingly, these agents appear preferable to currently available nonselective nonsteroidal anti-inflammatory drugs for use in patients at risk for upper gastrointestinal complications. Additionally, at doses recommended for treatment of osteoarthritis, both celecoxib and rofecoxib appear to be better tolerated, with a lower incidence of dyspepsia and other gastrointestinal side effects, than comparator nonselective nonsteroidal anti-inflammatory drugs. Like nonselective nonsteroidal anti-inflammatory drugs, however, cyclooxygenase 2-specific inhibitors can cause renal toxicity. Caution must be exercised, therefore, if they are used in patients with hypertension, congestive heart failure, or mild-to-moderate renal insufficiency; they should not be used in patients with severe renal insufficiency. In addition, the use of celecoxib is contraindicated in patients with a history of an allergic reaction to a sulfonamide.

An alternative to the use of cyclooxygenase 2-specific inhibitors is the use of nonselective nonsteroidal anti-inflammatory drugs with gastroprotective agents, as described in the 1995 American College of Rheumatology recommendations and endorsed by the American College of Gastroenterology. As noted above, serious adverse upper gastrointestinal events attributed to nonsteroidal anti-inflammatory drugs in the elderly are dose dependent. Therefore, if nonselective nonsteroidal anti-inflammatory drugs are used, they should be started in low, analgesic doses and increased to full antiinflammatory doses only if lower doses do not provide adequate symptomatic relief. In the patient who is at increased risk for a serious upper gastrointestinal adverse event, gastroprotective agents should be used even if nonselective nonsteroidal anti-inflammatory drugs are given at low dosage.

In a study of 8,843 patients with rheumatoid arthritis, 200 micrograms of misoprostol 4 times a day reduced the incidence of complicated ulcers, including those with perforation, bleeding, and obstruction, by 51%. In a 12-week, randomized, double-blind, placebo-controlled endoscopy study, 200 micrograms of misoprostol 3 times a day had comparable efficacy in preventing both gastric and duodenal ulcers; however, 200 micrograms of misoprostol twice a day conferred significantly less protection from gastric ulcers. Nonetheless, side effects, particularly diarrhea and flatulence, may occur with this agent, in a dose-dependent manner. Alternative approaches to prophylaxis with misoprostol include the use of high-dose famotidine or omeprazole, both of which have been shown to be effective in treating and preventing nonsteroidal anti-inflammatory drug gastropathy in carefully conducted endoscopy studies. H_2 blockers in usual doses, however, have not been found to be as effective as misoprostol. Either 20 mg/day or 40 mg/day omeprazole was as effective as 200 micrograms of misoprostol twice a day in the treatment of existing ulcers, and was better tolerated and associated with a lower rate of relapse. Proton pump inhibitors,

however, have not been approved by the U.S. Food and Drug Administration for use in prophylaxis, although they are being widely used for that purpose.

In addition to their effects on the gastrointestinal mucosa, nonselective nonsteroidal anti-inflammatory drugs inhibit platelet aggregation, further increasing the risk of gastrointestinal bleeding. Nonacetylated salicylates (e.g., choline magnesium trisalicylate, salsalate) are not accompanied by the antiplatelet effects or renal toxicity associated with nonselective nonsteroidal anti-inflammatory drugs, and can also be considered in management of the high-risk patient; however, ototoxicity and central nervous system toxicity at clinically efficacious doses may limit their use.

An alternative approach to the use of oral agents in the palliation of joint pain is the use of intraarticular therapy such as hyaluronan (hyaluronic acid) or glucocorticoids. Two preparations of intraarticular hyaluronan have been approved by the U.S. Food and Drug Administration for the treatment of knee osteoarthritis patients who have not responded to a program of nonpharmacologic therapy and acetaminophen. To date, differences in clinical efficacy between these preparations as a function of molecular weight have not been demonstrated. Because the duration of benefit reported for these agents exceeds their synovial half-life, their mechanisms of action are unclear; proposed mechanisms include inhibition of inflammatory mediators such as cytokines and prostaglandins, stimulation of cartilage matrix synthesis and inhibition of cartilage degradation, and a direct protective action on nociceptive nerve endings.

Intraarticular hyaluronan therapy is indicated for use in patients who have not responded to a program of nonpharmacologic therapy and simple analgesics; intraarticular hyaluronan injections may be especially advantageous in patients in whom nonselective nonsteroidal anti-inflammatory drugs and cyclooxygenase-2-specific inhibitors are contraindicated, or in whom they have been associated either with a lack of efficacy or with adverse events. Limited data are available concerning the effectiveness of multiple courses of intraarticular hyaluronan therapy. Transient mild-to-moderate pain at the injection site may occur; occasionally, mild-to-marked increases in joint pain and swelling have been noted following hyaluronan injection.

Intraarticular glucocorticoid injections are of value in the treatment of acute knee pain in patients with osteoarthritis, and may be particularly beneficial in patients who have signs of local inflammation with a joint effusion. When joints are painful and swollen, aspiration of fluid followed by intraarticular injection of a glucocorticoid preparation (e.g., up to 40 mg triamcinolone hexacetonide) is an effective short-term method of decreasing pain and increasing quadriceps strength. Injection can be used as monotherapy in selected patients or as an adjunct to systemic therapy with an analgesic, a nonselective nonsteroidal anti-inflammatory drug, or a cyclooxygenase 2-specific inhibitor. Joints should be aspirated/injected using aseptic technique, and the fluid should be sent for a cell count. Gram stain and culture should be performed if infection is suspected. Some patients may experience a mild flare of synovitis due to a reaction to the crystalline steroid suspensions; however, these postinjection flares are temporary and can be treated with analgesics and cold compresses. The risk of introducing infection into an osteoarthritis joint is exceedingly low if standard aseptic technique is used.

Tramadol, a centrally acting oral analgesic, is a synthetic opioid agonist that also inhibits reuptake of norepinephrine and serotonin. It has been approved by the U.S. Food and Drug Administration for the treatment of moderate-to-severe pain and can be considered for use in patients who have contraindications to cyclooxygenase 2-specific inhibitors and nonselective nonsteroidal anti-inflammatory drugs, including impaired renal function, or in patients who have not responded to previous oral therapy. Although there are numerous studies of the use of tramadol in general pain, few controlled studies have examined its use in osteoarthritis. The efficacy of tramadol has been found to be comparable with that of ibuprofen in patients with hip and knee osteoarthritis, and it has been found to be useful as adjunctive therapy in patients with osteoarthritis whose symptoms are inadequately controlled with nonsteroidal anti-inflammatory drugs. Mean effective daily doses of tramadol have generally been in the range of 200 to 300 mg, given in 4 divided doses. Side effects are common and include nausea, constipation, and drowsiness. Despite its opioid pharmacology, a comprehensive surveillance program has failed to demonstrate significant abuse, and tramadol remains an unscheduled agent.

Patients who do not respond to or cannot tolerate tramadol and who continue to have severe pain may be considered candidates for more potent opioid therapy. The American Pain Society and American Academy of Pain Medicine have published joint guidelines on the use of more potent opioids in the management of chronic, nonmalignant pain (American Academy of Pain Medicine and American Pain Society. The use of opioids for the treatment of chronic pain. Glenview [IL]: American Academy of Pain Medicine and American Pain Society, 1997).

Tolerance, dependence, and adverse effects, including respiratory depression and constipation, may occur with opioid usage.

Although the efficacy of therapy with combinations of the above pharmacologic agents has not been established in controlled clinical trials, in general, it is reasonable to use the recommended agents in combination in an individual patient. However, only a single nonsteroidal anti-inflammatory drug should be used at any given time, the sole exception being the concomitant use of a cardioprotective dose of aspirin (81 to 325 mg/day) with other nonsteroidal anti-inflammatory drugs. Even these low doses of aspirin, however, will increase the risk of upper gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs. In this regard, it should be noted that the incidence of endoscopically identified ulcers in patients taking a cyclooxygenase 2-specific inhibitor and a cardioprotective dose of aspirin was lower than that in comparator groups taking nonselective nonsteroidal anti-inflammatory drugs with or without concomitant low-dose aspirin.

Initiation of Treatment in the Patient who is not at Increased Risk for an Upper Gastrointestinal Adverse Event

The approach recommended for treatment of patients not at increased risk for an upper gastrointestinal adverse event is similar to that described above in the section titled "Pharmacologic Therapy for Patients with Osteoarthritis". As in the case of patients at increased risk for a serious upper gastrointestinal adverse event, if a nonselective nonsteroidal anti-inflammatory drug is used, it should be started at a low, analgesic dosage that should be increased only if it is ineffective

in providing symptomatic relief. Use of concomitant gastroprotective therapy with misoprostol or a proton pump inhibitor, however, is not recommended in the low-risk patient.

Management of Osteoarthritis in the Patient who is Already Taking a Nonsteroidal Anti-inflammatory Drug

The above sections address the management of osteoarthritis in patients who have not had prior treatment of their disease. In osteoarthritis patients who are already taking an nonsteroidal anti-inflammatory drug, but who have not incorporated relevant nonpharmacologic measures (e.g., an exercise program, weight loss program, adherence to principles of joint protection) into their treatment program, such measures should be implemented. This may permit reduction of the dosage of nonsteroidal anti-inflammatory drug or replacement of the nonsteroidal anti-inflammatory drug with acetaminophen. In all patients whose symptoms are well controlled, attempts should be made periodically to reduce the dosage of nonsteroidal anti-inflammatory drug and/or analgesic agents and to determine whether it is possible to use such agents on an as-needed basis, rather than in a fixed dosing regimen.

Tidal Irrigation

While the 1995 American College of Rheumatology guidelines recommended that tidal irrigation (TI) should be considered for those patients with knee osteoarthritis that did not respond satisfactorily to nonpharmacologic and pharmacologic measures, it was cautioned that information did not exist concerning the magnitude of the placebo response to this procedure. An ongoing, sham-controlled study of tidal irrigation is currently in progress, but results are not available. The placebo response to an invasive procedure, such as tidal irrigation, may be large, and results of properly controlled studies of tidal irrigation, which would permit guidance in this area, are not yet available. Accordingly, although some data suggest that tidal irrigation may be efficacious in some patients, the subcommittee believes that a statement concerning the role for this modality should await further study.

Treatment of the Patient with Hip Osteoarthritis

It should be noted that therapy for osteoarthritis of the hip is similar to treatment of osteoarthritis of the knee, except for a few minor differences. Intraarticular hyaluronan therapy is not approved for hip osteoarthritis, and there are no published studies regarding its efficacy in patients with hip osteoarthritis. Topical agents have not been studied in hip osteoarthritis, and their efficacy is questionable because of the depth of that joint. Intraarticular glucocorticoid injections have not been studied in patients with hip osteoarthritis, but are used occasionally and may be efficacious. Injections performed without fluoroscopic guidance should be administered only by those experienced in this approach. Modalities of physical therapy for patients with hip osteoarthritis differ from those used in patients with osteoarthritis of the knee. Consultation with a physical therapist should be considered as part of the overall management.

Surgical Treatment

Patients with severe symptomatic osteoarthritis who have pain that has failed to respond to medical therapy and who have progressive limitation in activities of daily living should be referred to an orthopedic surgeon for evaluation. No well-controlled trials of arthroscopic debridement with or without arthroplasty have been conducted, and the utility of this intervention for the treatment of knee osteoarthritis is unproven. In appropriately selected patients who are not yet candidates for total joint arthroplasty, osteotomy may provide pain relief and prevent progression of disease. Total joint arthroplasty provides marked pain relief and functional improvement in the vast majority of patients with osteoarthritis, and has been shown to be cost effective in selected patients. Indications for total hip replacement, developed at a U.S. National Institutes of Health (NIH) Consensus Conference (NIH Consens Statement 1994 Sep 12-14;12[5]:1-31), include "radiographic evidence of joint damage and moderate to severe persistent pain or disability, or both, that is not substantially relieved by an extended course of nonsurgical management." While there are no published evidence-based indications for total knee replacement, Dieppe and colleagues have summarized the indications derived from 3 consensus groups of orthopedic surgeons (Dieppe P, Basler HD, Chard J, Croft P, Dixon J, Hurley M, et al. Knee replacement surgery for osteoarthritis: effectiveness, practice variations, indications and possible determinants of utilization. Rheumatology 1999;38:73-83).

Outcomes depend upon the timing of the surgery, the experience of the surgeon and the hospital with the procedure, and the patient's preoperative medical status, peri- and postoperative management, and rehabilitation.

Agents Under Investigation

While a number of studies support the efficacy of both glucosamine and chondroitin sulfate for palliation of joint pain in patients with knee osteoarthritis, the subcommittee believes that it is premature to make specific recommendations about their use at this time because of methodologic considerations, including lack of standardized case definitions and standardized outcome assessments, as well as insufficient information about study design in a number of these published reports. A pivotal clinical trial being planned by the U.S. National Institutes of Health should help define the role of these agents, singly and in combination, in the treatment of patients with knee osteoarthritis.

In addition, currently existing data are insufficient or inadequate to permit the subcommittee to make definitive recommendations about the use of devices, such as pulsed electromagnetic fields and lasers. Further research is needed on vitamin deficiencies, which have been suggested as possible causes of (or aggravating factors in) osteoarthritis, before dietary supplementation can be recommended for prevention or treatment of this disease. Similarly, the value, if any, of other nutritional supplements, including supraphysiologic doses of anti-oxidant vitamins, remains to be determined.

In addition, therapeutic approaches such as acupuncture are difficult to evaluate and recommend because of large placebo effects of invasive procedures and the lack of adequate sham-controlled studies. An ongoing, pivotal, randomized, sham-controlled trial of acupuncture, supported by the U.S. National Institutes of

Health, is under way; this trial should help define acupuncture's role in the treatment of patients with knee osteoarthritis.

The 1995 American College of Rheumatology recommendations briefly mentioned preliminary studies of disease-modifying osteoarthritis drugs (DMOADs), drugs whose action is not aimed principally at the control of symptoms, but instead at the prevention of structural damage in normal joints at risk for development of osteoarthritis, or at the progression of structural damage in joints already affected by osteoarthritis. For the most part, such approaches have been aimed at inhibiting the breakdown of articular cartilage by matrix metalloproteinases, or at stimulating repair activity by chondrocytes. Although a number of agents are under study, including matrix metalloproteinase inhibitors and growth factors, no agent has been shown to have a disease-modifying osteoarthritis drugs effect in humans, and none are available for this indication.

In addition to therapeutic agents targeted toward prevention, retardation, or reversal of cartilage breakdown in osteoarthritis, significant advances, such as autologous chondrocyte transplantation, cartilage repair using mesenchymal stem cells, and autologous osteochondral plugs (mosaicplasty), are being investigated for repair of focal chondral defects. These procedures are not currently indicated in the treatment of patients with osteoarthritis.

Given the advances in therapy that can be anticipated for patients with osteoarthritis, the subcommittee expects that current recommendations will change as new knowledge of the disease unfolds and new therapies become available.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation. However, data from systematic reviews, meta-analyses, and published findings of randomized controlled trials as well as data from randomized controlled trials presented as abstracts at scientific meetings were used to support the recommendations. Where such data were not available, expert opinion was used.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

The goals of the contemporary management of the patient with osteoarthritis continue to include control of pain and improvement in function and health-related quality of life, with avoidance, if possible, of toxic effects of therapy.

POTENTIAL HARMS

There is potential for adverse effects of drugs and injections:

- Acetaminophen. Acetaminophen can prolong the half-life of warfarin sodium. Careful monitoring of the prothrombin time is recommended in patients taking warfarin sodium who subsequently begin high-dose acetaminophen treatment. Hepatic toxicity with acetaminophen is rare with doses of ≤4 gm/day. Nonetheless, acetaminophen should be used cautiously in patients with existing liver disease and avoided in patients with chronic alcohol abuse because of known increased risk in these settings. Even though acetaminophen was reported to be weakly associated with end-stage renal disease, the Scientific Advisory Committee of the National Kidney Foundation recommends it as the drug of choice for analgesia in patients with impaired renal function.
- Nonsteroidal anti-inflammatory drugs. Potential adverse effects include serious upper gastrointestinal (GI) and renal toxicity.
- Cyclooxygenase 2 (COX-2)-specific inhibitors. Cyclooxygenase 2-specific inhibitors can cause renal toxicity.
- Tramadol. Side effects are common and include nausea, constipation, and drowsiness.
- Intraarticular hyaluronan injections. Transient mild-to-moderate pain at the injection site may occur; occasionally, mild-to-marked increases in joint pain and swelling have been noted following hyaluronan injection.

Subgroups Most Likely to be Harmed:

Risk factors for upper gastrointestinal bleeding in patients treated with nonsteroidal anti-inflammatory drugs include:

- Age 65 years and older
- History of peptic ulcer disease or of upper gastrointestinal bleeding
- Concomitant use of oral glucocorticoids or anticoagulants
- Presence of comorbid conditions, and, possibly
- Smoking and alcohol consumption

Risk factors for reversible renal failure in patients with intrinsic renal disease (usually defined as a serum creatinine concentration of ≥2.0 mg/dl) who are treated with nonsteroidal anti-inflammatory drugs include:

- Age 65 years and older
- Hypertension and/or congestive heart failure
- Concomitant use of diuretics and angiotensin-converting enzyme inhibitors

Caution must be exercised if cyclooxygenase 2-specific inhibitors are used in patients with hypertension, congestive heart failure, or mild-to-moderate renal insufficiency; they should not be used in patients with severe renal insufficiency. In addition, the use of celecoxib is contraindicated in patients with a history of an allergic reaction to a sulfonamide.

If nonselective nonsteroidal anti-inflammatory drugs are used, they should be started in low, analgesic doses and increased to full antiinflammatory doses only if lower doses do not provide adequate symptomatic relief. In the patient who is at increased risk for a serious upper gastrointestinal adverse event, gastroprotective agents should be used even if nonselective nonsteroidal anti-inflammatory drugs are given at low dosage.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The American College of Rheumatology Subcommittee on Osteoarthritis Guidelines emphasizes that these recommendations are not fixed, rigid mandates, and recognizes that the final decision concerning the therapeutic regimen for an individual patient rests with the treating physician.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Recommendations for the medical management of osteoarthritis of the hip and knee: 2000 update. American College of Rheumatology Subcommittee on Osteoarthritis Guidelines. Arthritis Rheum 2000 Sep;43(9):1905-15. [91 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Sep

GUIDELINE DEVELOPER(S)

American College of Rheumatology - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Rheumatology (ACR)

GUIDELINE COMMITTEE

Subcommittee on Osteoarthritis Guidelines

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Subcommittee Members: Roy D. Altman, MD; Marc C. Hochberg, MD, MPH; Roland W. Moskowitz, MD; Thomas J. Schnitzer, MD, PhD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Subcommittee have relationships with the following pharmaceutical or biotechnology companies. Roy D. Altman, MD: Abbott, Aventis Pharmaceutical Co., BoehringerIngelheim, Eutovita, Fidia Co., Johnson & Johnson, Ortho-McNeil, Merck Sharp and Dohme, Novartis, Pierre Farber, Procter and Gamble, Sanofi, Searle, United Therapeutics, Whitehall Robbins, Negma, and NeuColl Corp. Marc C. Hochberg, MD, MPH: Merck & Co., Aventis Pharmaceutical Co., NEGMA Laboratories, Procter and Gamble, Roche, Wyeth-Ayerst, Johnson & Johnson, Eli Lilly, and Schering Plough. Roland W. Moskowitz, MD: Searle (Pharmacia), Sanofi-Synthelab, Fidia Co., and NeuColl Corp. Thomas J. Schnitzer, MD, PhD: Abbott, Boehringer-Ingelheim, Johnson & Johnson, McNeil Consumer, Merck & Co., Novartis, Ortho-McNeil, Parke-Davis, Searle, Wyeth-Ayerst, and SmithKline Beecham.

GUIDELINE STATUS

This is the current release of the guideline. This guideline updates two previously released guidelines:

- Guidelines for the medical management of osteoarthritis. Part I. Osteoarthritis of the hip. Arthritis Rheum 1995 Nov;38(11):1535-40.
- Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. Arthritis Rheum 1995 Nov;38(11):1541-6

GUIDELINE AVAILABILITY

Electronic copies: Available from the American College of Rheumatology (ACR) Web site.

Print copies: Available from the American College of Rheumatology, 1800 Century Place, Suite 250, Atlanta, GA 30345.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Guidelines for the development of practice guidelines. Atlanta (GA): American College of Rheumatology, 1998. 4 p. Electronic copies available from the American College of Rheumatology Web site.

Print copies: Available from the American College of Rheumatology, 1800 Century Place, Suite 250, Atlanta, GA 30345.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on October 17, 2001. The information was verified by the guideline developer as of May 8, 2002.

COPYRIGHT STATEMENT

Date Modified: 5/10/2004